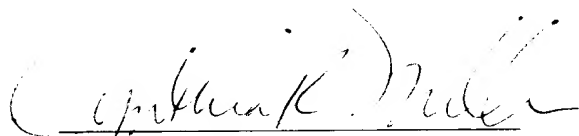


Remarks

The above amendatory action is requested to comply with the applicable Sequence Listing requirements. A computer readable copy of the Sequence Listing and the requisite Statements are submitted herewith. The above amendatory action also is requested to make changes of an editorial and clerical nature.

The additional claim fee also is submitted herewith.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

The following heading has been inserted before paragraph beginning at line 18 on page 6.

DETAILED DESCRIPTION

Paragraph beginning at line 18 on page 6 has been amended as follows:

[Figure 3. Whole] SEQ. ID NO:1 is a whole nucleotide sequence of human hepatitis B virus, isolated from an eleven year old child born to a mother in Singapore with the wild type virus. The child had received standard Hepatitis B immunoglobulin (HBIG) and HB vaccine and was infected with the mutated strain one year later. This strain carries a mutation at amino acid residue 145 (glycine to arginine) of the major surface antigen (SEQ. I.D. No. 1). The mutation is shown at nucleic acids numbered 587-589.

Paragraph beginning at line 30 on page 6 has been amended as follows:

[Figure 4. Deduced] SEQ ID NO:2 is the deduced amino acid sequence of the DNA polymerase from the nucleotide sequence of [Figure 3 (]SEQ[.] I[.]D[.] N[o]O:1 [2)].

Paragraph beginning at line 34 on page 6 has been amended as follows:

[Figure 5. Deduced] SEQ ID NO:3 is the deduced amino acid sequence of the large surface antigen from the nucleotide sequence of [figure 3) SEQ ID NO:1. The mutated amino acid residue (G to R) is numbered 319 [(SEQ. I.D. No. 3)].

Paragraph beginning at line 1 on page 7 has been amended as follows:

[Figure 6. Deduced] SEQ ID NO:4 is the deduced amino acid sequence of the core protein from the nucleotide sequence of [Figure 3 (]SEQ[.] I[.]D[.] N[o]O:1 [4)].

Paragraph beginning at line 5 on page 7 has been amended as follows:

[Figure 7. Deduced] SEQ ID NO:5 is the deduced amino acid sequence of the trans-activating X protein from the nucleotide sequence of [Figure 3 (]SEQ[.] I[.]D[.] N[o]O:1 [5)].

Paragraph beginning at line 10 on page 7 has been amended as follows:

[Figure 8. Oligonucleotide] SEQ ID NO:6 is the oligonucleotide sequence corresponding to the initiation site of the coding region of DNA polymerase, at position 2307 of the viral genome and matches the coding strand (sense oligonucleotide) [(SEQ. I.D. No. 6)].

Paragraph beginning at line 16 on page 7 has been amended as follows:

[Figure 9. Oligonucleotide] SEQ ID NO:7 is the oligonucleotide sequence corresponding to position 250 of the viral nucleotide sequence and matches the complementary strand (anti-sense oligonucleotide) [(SEQ. I.D. No. 7)].

Paragraph beginning at line 21 on page 7 has been amended as follows:

[Figure 10. Oligonucleotide] SEQ ID NO:8 is the oligonucleotide sequence corresponding to position 250 of the viral nucleotide sequence and matches the coding strand (sense oligonucleotide) [(SEQ. I.D. No. 8)].

Paragraph beginning at line 26 on page 7 has been amended as follows:

[Figure 11. Oligonucleotide] SEQ ID NO:9 is the oligonucleotide sequence corresponding to the stop codon of the coding region of DNA polymerase, at position 1623 of the viral genome and matches the complementary strand (anti-sense oligonucleotide) [(SEQ. I.D. No. 9)].

Paragraph beginning at line 32 on page 7 has been amended as follows:

[Figure 12. Oligonucleotide] SEQ ID NO:10 is the oligonucleotide sequence corresponding to position 1420 of the viral genome and matches the coding strand (sense oligonucleotide) [(SEQ. I.D. No.10)].

Paragraph beginning at line 37 on page 7 has been amended as follows:

[Figure 13. Oligonucleotide] SEQ ID NO:11 is the oligonucleotide sequence corresponding to position 2340 of the viral genome and matches the complementary strand (anti-sense oligonucleotide) [(SEQ. I.D. No. 11)].

Paragraph beginning at line 12 on page 9 has been amended as follows:

The present invention provides the nucleotide sequence of a hepatitis B virus genome, which carries a vaccine-induced mutation at amino acid residue 145 (Glycine to Arginine) of the major surface antigen, consisting of 3215 nucleotides [Figure 3] (SEQ ID NO:1) coding for 4 overlapping viral proteins [shown in Figures 4-7].

Paragraph beginning at line 35 on page 29 has been amended as follows:

From the analysis described above, the full-length nucleotide sequence of the hepatitis B virus carrying a vaccine-induced mutation at amino acid residue 145 (Glycine to Arginine) of the major surface antigen was determined as shown in [Figure 3] SEQ ID NO:1.

Paragraph beginning at line 1 on page 30 has been amended as follows:

The deduced amino acid sequences coding for the major viral proteins are shown in Figures 4-7: hepatitis B viral DNA polymerase [(Figure 4)] (SEQ ID NO:2), the large surface antigen [(Figure 5)] (SEQ ID NO:3), the core protein [(Figure 6)] (SEQ ID NO:4) and the trans-activating X protein [(Figure 7)] (SEQ ID NO:5).